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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/830,548 | 06/12/2001 | Katsunari Tezuka | 06501-077001 | 9334 |

7590 06/13/2003

Janis K Fraser
Fish & Richardson
225 Franklin Street
Boston, MA 02110-2804

| EXAMINER |
|---|
| ROARK, JESSICA H |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | 27 |

DATE MAILED: 06/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 09/830,548 | TEZUKA ET AL. | |
| | Examin r | Art Unit | |
| | Jessica H. Roark | 1644 | |

*-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 23-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11,19* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-32 are pending.

2. Applicant's election of Group V with a species election of antibody in Paper No. 22 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

*After further consideration and in view of the rejections set forth herein, Groups VII and IX have been rejoined to Group V and are fully considered herein.*

Claims 1-17 and 23-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

*Claims* 18-22 *are under consideration in the instant application.*

3. In order to facilitate the prosecution of this application, Applicant is requested to cancel all non-elected embodiments from the claims, e.g., sections b)-d) in claim 22.

***Drawings***

4. The drawings submitted 1/2/02 have been approved by the Draftsman.

***Priority***

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

**IDS**

6. Applicant's IDSs, filed 6/18/02 and 2/14/03 (Paper Nos. 11 and 19), are acknowledged.

The Declaration of Dr. Katsunari Tezuka that the copies of the poster of IDS #APP, as well as copies of a poster associated with the abstract of IDS #AXX, were distributed to neither the organizer nor attendees of the respective conferences is acknowledged.

***Specification***

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

9. For examination purposes, it is noted that the specification defines "AILIM" on page 17 to encompass a genus of polypeptides known in the art for human, mouse and rat and variants thereof. For example, the specification discloses on page 17 that human AILIM includes the human 8F4 polypeptide of WO99/15553 (of record). It is further noted that although the "AILIM" polypeptide is also commonly known in the art as "ICOS", the term "AILIM" at the time the invention was made was also an art-recognized term (see e.g. Tamatani et al. Int. Immunol. 2000; 12(1):51-55 and Tezuka et al. Biochem. Biophys. Res. Com. 2000; 276(1):335-345, IDS#AZZ).

***Claim Rejections - 35 USC § 112 first paragraph***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

11. Claims 18-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

The claims recite a method comprising administering "a substance that modulates signal transduction mediated by AILIM" as part of the invention.

The specification discloses on pages 21 that "a substance that modulates signal transduction mediated by AILIM" is essentially any natural or artificially prepared substance that by any mechanism results in the modulation of signal transduction through AILIM. The specification discloses that such a substance may be an antibody to AILIM, the extracellular domain or fusion polypeptides comprising AILIM, polypeptides that bind AILIM (e.g., B7RP-1), DNA, RNA or chemically synthesized compounds.

Thus the genus of substances that "modulate signal transduction mediated by AILIM" is highly variable.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. (See MPEP 2163 II.ii).

The specification further discloses individual species of substances which are antibodies to AILIM, the extracellular domain or fusion polypeptides comprising AILIM, and the AILIM ligand B7-RP-1.

The specification therefore only appears to provide a limited number of species with the recited function. Given that substances having any structure are encompassed by the instant methods, so long as the substance interacts with the AILIM signal transduction pathway at any point to modulate it; the instant species do not appear to sufficiently reflect the variation within the genus.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

***Claim Rejections – 35 U.S.C. §§ 102 and 103***

12. For examination purposes under 35 USC 102 and 103, the claims are considered as limited to the elected species of an antibody to AILIM.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

*(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

*(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.*

14. Claim 18-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Kroczek (DE 198 21 060 A1, laid open 14 April 1999, of record, see entire document), as evidenced by the definition of "AILIM" in the specification on page 17.

Kroczek teaches an antibody to the 8F4 polypeptide (see entire document). The 8F4 polypeptide is a human AILIM polypeptide as evidenced by the definition of AILIM on page 17 of the specification.

Kroczek also teaches that antibodies to the 8F4 polypeptide can be used as a pharmaceutical compositions to blockade the interaction of the 8F4 antigen with its receptor in methods of preventing rejection reactions in organ transplants (see e.g., page 12 of translation). Pharmaceutical compositions of antibodies necessarily comprise a pharmaceutically acceptable carrier.

A blocking antibody to the 8F4 polypeptide is a protein that modulates signal transduction by AILIM, including proliferation and cytokine production, because Kroczek further teaches that the 8F4/AILIM polypeptide stimulates proliferation of T lymphocytes and enhances production of certain cytokines (see page 8 of translation). Although Kroczek is silent as to the inhibition of the cytokines interferon γ and interleukin 4 by antibodies to 8F4/AILIM, the individual cytokines inhibited would be inherent in any method comprising contacting AILIM/8F4 in vivo with a blocking antibody.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent in methods of preventing rejection reactions in organ transplants using the anti-8F4 antibody of Kroczek.

The reference teachings thus anticipate the instant claimed invention.

15. Claims 18-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Coyle et al. (US 2002/0164697, see entire document), as evidenced by the definition of "AILIM" in the specification on page 17.

Coyle et al. teach a human TH2-specific polypeptide "h1228" (see entire document). Coyle et al. acknowledge the h1228 polypeptide is a human ICOS polypeptide (see entire document, but especially the comments at paragraph 27 and SEQ ID NO:12). ICOS is another name for an AILIM polypeptide, as evidenced by the definition of AILIM in the specification on page 17.

Coyle et al. teach human antibodies which bind "h1228" and their formulation as pharmaceutical compositions comprising the antibody and a pharmaceutically acceptable carrier (see especially paragraphs 102-110 and 127-141).

Coyle et al. teach that antibodies to h1228/AILIM can be used to inhibit one or more biological activities of the h1228/AILIM polypeptide (see e.g., paragraph 41). "Biological activities" of the TH2 polypeptides are taught at paragraph 41 to encompass direct and indirect effects of cellular signaling activities mediated by h1228/AILIM, including proliferation of TH2-type cells and cytokine production, including IL-4 production, by TH2-type cells.

Coyle et al. also teach that antibodies (i.e., a composition for modulation of the immune response) can be used to treat immune disorders including graft rejection and graft versus host disease (see e.g., paragraph 38 in view of paragraph 41)

It is acknowledged that the h1228 polypeptide of Coyle et al. has an amino acid deletion at position 166 compared to the human AILIM polypeptides referenced in the specification on page 17. However, it is noted that the definition of AILIM in the specification also encompasses AILIM polypeptides having amino acid deletions. In addition, the human anti-h1228 antibody of Coyle et al. would *inherently* bind the human AILIM polypeptides referenced in the specification on page 17 given the shared antibody epitopes.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent in methods of treating immune disorders including graft rejection and graft versus host disease using the anti-h1228 antibody of Coyle et al.

The reference teachings thus anticipate the instant claimed invention.

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

*(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kroczek (DE 198 21 060 A1, laid open April 15, 1999; translation provided, of record) and Linsley et al. (U.S. Pat. No. 5,770,197), as evidenced by Applicant's definition of "AILIM" on page 17 of the specification.

The claims are drawn to methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction by administering an antibody to AILIM.

Kroczek teaches an antibody to the 8F4 polypeptide (see entire document). The 8F4 polypeptide is a human AILIM polypeptide as evidenced by the definition of AILIM on page 17 of the specification.

Kroczek teaches that the 8F4/AILIM polypeptide stimulates proliferation of T lymphocytes and enhances production of certain cytokines (see page 8 of translation). Kroczek also teaches that antibodies to the 8F4 polypeptide can be used as a pharmaceutical composition to blockade the interaction of the 8F4 antigen with its receptor, and that this blockade can be used as a method of preventing rejection reactions in organ transplants (see e.g., page 12 of translation).

Kroczek does not teach methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction by administering an antibody to AILIM.

Linsley et al. teach and claim methods of inhibiting both tissue transplant rejection and graft versus host disease by administering a combination of a B7-binding molecule that is CTLA4Ig and an antibody to IL-4 (see entire document, especially the claims). Linsley et al. teach that CTLA4Ig inhibits the interaction of B7 with CD28 on T cells better than anti-CD28 antibodies, and that the B7:CD28 interaction leads to cytokine production and T cell proliferation, which in turn are involved in allograft rejection and graft versus host disease (see e.g., "USES" at columns 13-16). Linsley et al. teach that CTLA4Ig may be used alone or in combination with other immunosuppressants that block T cell proliferation in treating graft versus host disease (e.g., column 16, especially lines 18-21).

Thus Linsley et al. teach that reagents which inhibit T cell proliferation can be used in methods of treating both graft versus host disease and immune rejection of transplanted tissues or organs.

It would therefore have been obvious to the ordinary artisan at the time the invention was made that other molecules which antagonize T cell proliferation and cytokine production, particularly the production of TH2 cytokines such as IL-4, could be used in methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction either in place of or in combination with the CTLA4Ig and anti-IL-4 antibody reagents taught by Linsley et al.

Given the teachings of Kroczek et al. that 8F4 is a molecule which stimulates T cell proliferation and cytokine production, and the teachings of Kroczek that antibodies to the 8F4/AILIM polypeptide can be used to prevent rejection of organ transplants; the ordinary artisan at the time the invention was made would have found it obvious to substitute or combine the anti-8F4 antibody of Kroczek with the CTLA4Ig and anti-IL-4 antibody therapy of Linsley et al. for preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction.

The ordinary artisan at the time the invention was made would have been motivated to combine the antibody to 8F4 taught by Kroczek with the CTLA4Ig/anti-IL-4 therapy taught by Linsley et al. because Linsley et al. teach that combination therapy with other reagents that inhibit T cell proliferation is routine practice in the art.

Alternatively, substitution of a single anti-8F4 reagent that functioned as well as multiple reagents would have been highly desirable as a means of reducing both the cost and complications associated with administering multiple reagents. Thus the ordinary artisan at the time the invention was made would have been motivated to substitute the anti-8F4 antibody taught by Kroczek for the CTLA4Ig/anti-IL-4 antibody therapy of Linsley et al. in order to ascertain if a single reagent, an anti-8F4/AILIM antibody, would function as well as the combination taught by Linsley et al. in a method of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction.

Given the teachings of Kroczek that the anti-8F4 antibody could be used to inhibit proliferation of T cells and could be used to inhibit rejection reactions associated with transplantation, the ordinary artisan at the time the invention was made would have had a reasonable expectation that an antibody to 8F4/AILIM could also be used in a method of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction.

Although Kroczek is silent as to the inhibition of the cytokines interferon γ and interleukin 4 by antibodies to 8F4/AILIM, the individual cytokines interferon γ and interleukin 4 would necessarily be inhibited in any method comprising contacting AILIM/8F4 in vivo with a blocking antibody. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. Claims 18-22 are rejected under 35 U.S.C. 103(a) as being obvious over *any one of* US 2002/0115831, US 2002/0151685, US 2002/0156242 or US 2003/0083472 ("the published references") and Linsley et al. (U.S. Pat. No. 5,770,197), as evidenced by the definition of AILIM on page 17 of the instant specification.

The applied references each have a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). *For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, **at the time the invention was made**, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).*

It is noted that each of the published references are related as continuations or divisionals to the same parent applications; thus the disclosure of each is identical. Paragraph references will be provided only for one of these references, but the comments apply equally to all of the published references.

The claims are drawn to methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ by administering an antibody to AILIM.

Each of the published references teaches an antibody to a human JTT-1 antigen (see entire document of each). The JTT-1 antigen is a human AILIM polypeptide as evidenced by the definition of AILIM on page 17 of the instant specification.

Each of the published references teaches that the JTT-1 antigen provides a costimulatory signal essential for the activation of T lymphocytes (see e.g., paragraphs 533-538 of US 2002/0151685). Activated T lymphocytes are disclosed to secrete various cytokines and to proliferate (see e.g., paragraphs 110-112 of US 2002/0151685). Each of the published references also teaches that antibodies to the JTT-1 antigen can be used as a pharmaceutical composition for the therapy or prevention of diseases caused by the activation of T lymphocytes or the abnormality of regulation of activated lymphocyte function (see e.g., paragraphs 533-538 of US 2002/0151685).

None of the published references teaches methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ by administering an antibody to the JTT-1 antigen (AILIM).

Linsley et al. teach and claim methods of inhibiting both tissue transplant rejection and graft versus host disease by administering a combination of a B7-binding molecule that is CTLA4Ig and an antibody to IL-4 (see entire document, especially the claims). Linsley et al. teach that CTLA4Ig inhibits the interaction of B7 with CD28 on T cells better than anti-CD28 antibodies, and that the B7:CD28 interaction leads to cytokine production and T cell proliferation, which in turn is involved in allograft rejection and graft versus host disease (see e.g., "USES" at columns 13-16). Linsley et al. teach that CTLA4Ig may be used alone or in combination with other immunosuppressants that block T cell proliferation in treating graft versus host disease (e.g., column 16, especially lines 18-21).

Thus Linsley et al. teach that reagents which inhibit T cell proliferation can be used in methods of treating both graft versus host disease and immune rejection of transplanted tissues or organs.

It would therefore have been obvious to the ordinary artisan at the time the invention was made that other molecules which antagonize T cell proliferation and cytokine production (i.e., T lymphocyte activation), could be used in methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ either in place of or in combination with the CTLA4Ig and anti-IL-4 antibody reagents taught by Linsley et al.

Given the teachings of each of the published references that the JTT-1 antigen is a polypeptide involved in T cell proliferation and cytokine production, and the teachings of each of each of the published references that antibodies to the JTT-1/AILIM polypeptide can be used in the therapy or prevention of diseases caused by the activation of T lymphocytes or the abnormality of regulation of activated lymphocyte function; the ordinary artisan at the time the invention was made would have found it obvious to substitute or combine an antibody to the human JTT-1/AILIM polypeptide as taught by each of the published references with the CTLA4Ig and anti-IL-4 antibody therapy of Linsley et al. for preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ.

The ordinary artisan at the time the invention was made would have been motivated to combine the antibody to JTT-1/AILIM taught by each of the published references with the CTLA4Ig/anti-IL-4 therapy taught by Linsley et al. because Linsley et al. teach that combination therapy with other reagents that inhibit T cell proliferation is routine practice in the art.

Alternatively, substitution of a single anti-JTT-1/AILIM reagent that functioned as well as multiple reagents would have been highly desirable as a means of reducing both the cost and complications associated with administering multiple reagents. Thus the ordinary artisan at the time the invention was made would have been motivated to substitute the anti-JTT-1/AILIM antibody taught by each of the published references for the CTLA4Ig/anti-IL-4 antibody therapy of Linsley et al. in order to ascertain if a single reagent, an anti-JTT-1/AILIM antibody, would function as well as the combination taught by Linsley et al. in a method of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction.

Given the teachings of each of the published references that the anti-JTT-1 antibody could be used in the therapy or prevention of diseases caused by the activation of T lymphocytes or the abnormality of regulation of activated lymphocyte function; the ordinary artisan at the time the invention was made would have had a reasonable expectation that an antibody to JTT-1/AILIM could also be used in a method of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ.

Although each of the published references is silent as to the inhibition of the cytokines interferon $\gamma$ and interleukin 4 by antibodies to JTT-1/AILIM, the individual cytokines interferon $\gamma$ and interleukin 4 would necessarily be inhibited in any method comprising contacting AILIM/JTT-1 in vivo with an antibody that inhibited activated T cells. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. Claims 18-22 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over *either* copending Application No. 09/383,551 *or* copending Application No. 09/561,308, each of which has a common inventor with the instant application, and Linsley et al. (U.S. Pat. No. 5,770,197) as evidenced by the definition of AILIM on page 17 of the instant specification.

*Based upon the earlier effective U.S. filing date of each copending application, it would constitute prior art under 35 U.S.C. 102(e) if published or patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future publication or patenting of the conflicting application.*

The claims are drawn to methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ by administering an antibody to AILIM.

Each of USSN 09/383,551 and USSN 09/561,308 teaches an antibody to a human JTT-1 antigen (see entire document of each). The JTT-1 antigen is a human AILIM polypeptide as evidenced by the definition of AILIM on page 17 of the instant specification.

Each of USSN 09/383,551 and USSN 09/561,308 teaches that the JTT-1 antigen provides a costimulatory signal essential for the activation of T lymphocytes (see e.g., pages 114-115 of USSN 09/561,308). Activated T lymphocytes are disclosed to secrete various cytokines and to proliferate (see e.g. page 29 of USSN 09/561,308). Each of USSN 09/383,551 and USSN 09/561,308 also teaches that antibodies to the JTT-1 antigen can be used as a pharmaceutical composition for the therapy or prevention of diseases caused by the activation of T lymphocytes or the abnormality of regulation of activated lymphocyte function (see e.g., bridging paragraph of pages 114-115 of USSN 09/561,308).

Neither of USSN 09/383,551 or USSN 09/561,308 teaches methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ by administering an antibody to the JTT-1 antigen (AILIM).

Linsley et al. teach and claim methods of inhibiting both tissue transplant rejection and graft versus host disease by administering a combination of a B7-binding molecule that is CTLA4Ig and an antibody to IL-4 (see entire document, especially the claims). Linsley et al. teach that CTLA4Ig inhibits the interaction of B7 with CD28 on T cells better than anti-CD28 antibodies, and that the B7:CD28 interaction leads to cytokine production and T cell proliferation, which in turn is involved in allograft rejection and graft versus host disease (see e.g., "USES" at columns 13-16). Linsley et al. teach that CTLA4Ig may be used alone or in combination with other immunosuppressants that block T cell proliferation in treating graft versus host disease (e.g., column 16, especially lines 18-21).

Thus Linsley et al. teach that reagents which inhibit T cell proliferation can be used in methods of treating both graft versus host disease and immune rejection of transplanted tissues or organs.

It would therefore have been obvious to the ordinary artisan at the time the invention was made that other molecules which antagonize T cell proliferation and cytokine production (i.e., T lymphocyte activation), could be used in methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ either in place of or in combination with the CTLA4Ig and anti-IL-4 antibody reagents taught by Linsley et al.

Given the teachings of each of USSN 09/383,551 or 09/561,308 that the JTT-1 antigen is a polypeptide involved in T cell proliferation and cytokine production, and the teachings of each of USSN 09/383,551 and 09/561,308 that antibodies to the JTT-1/AILIM polypeptide can be used in the therapy or prevention of diseases caused by the activation of T lymphocytes or the abnormality of regulation of activated lymphocyte function; the ordinary artisan at the time the invention was made would have found it obvious to substitute or combine an antibody to the human JTT-1/AILIM polypeptide as taught by both USSN 09/383,551 and 09/561,308 with the CTLA4Ig and anti-IL-4 antibody therapy of Linsley et al. for preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ.

The ordinary artisan at the time the invention was made would have been motivated to combine the antibody to JTT-1/AILIM taught by each of USSN 09/383,551 and USSN 09/561,308 with the CTLA4Ig/anti-IL-4 therapy taught by Linsley et al. because Linsley et al. teach that combination therapy with other reagents that inhibit T cell proliferation is routine practice in the art.

Alternatively, substitution of a single anti-JTT-1/AILIM reagent that functioned as well as multiple reagents would have been highly desirable as a means of reducing both the cost and complications associated with administering multiple reagents. Thus the ordinary artisan at the time the invention was made would have been motivated to substitute the anti-JTT-1/AILIM antibody taught by each of USSN 09/383,551 and 09/561,308 for the CTLA4Ig/anti-IL-4 antibody therapy of Linsley et al. in order to ascertain if a single reagent, an anti-JTT-1/AILIM antibody, would function as well as the combination taught by Linsley et al. in a method of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction.

Given the teachings of both USSN 09/383,551 and USSN 09/561,308 that the anti-JTT-1 antibody could be used in the therapy or prevention of diseases caused by the activation of T lymphocytes or the abnormality of regulation of activated lymphocyte function; the ordinary artisan at the time the invention was made would have had a reasonable expectation that an antibody to JTT-1/AILIM could also be used in a method of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ.

Although each of USSN 09/383,551 and USSN 09/561,308 are silent as to the inhibition of the cytokines interferon γ and interleukin 4 by antibodies to JTT-1/AILIM, the individual cytokines interferon γ and interleukin 4 would necessarily be inhibited in any method comprising contacting AILIM/JTT-1 in vivo with an antibody that inhibited activated T cells. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

*This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were,* ***at the time the invention was made,*** *owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).*

***Double Patenting***

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

21. Claims 18-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 55-63 and 90-94 of copending Application No. 09/383,551 in view of Linsley et al. (U.S. Pat. No. 5,770,197), as evidenced by the definition of AILIM on page 17 of the instant specification.

The claims are drawn to methods of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ by administering an antibody to AILIM.

USSN 09/383,551 claims generic methods of inhibiting activation of lymphocytes in a subject by administering a composition comprising an antibody to the polypeptide of SEQ ID NO:2 and a pharmaceutically acceptable carrier. SEQ ID NO:2 is an AILIM polypeptide as evidenced by the definition of an AILIM polypeptide on page 17 of the instant specification. The disclosure of USSN 09/383,551 defines an activated T lymphocyte as one which secretes various cytokines and proliferates (see e.g. page 29).

USSN 09/383,551 does not claim the specific method of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ by administering an antibody to AILIM.

Linsley et al. teach and claim methods of inhibiting both tissue transplant rejection and graft versus host disease by administering a combination of a B7-binding molecule that is CTLA4Ig and an antibody to IL-4 (see entire document, especially the claims). Linsley et al. teach that CTLA4Ig inhibits the interaction of B7 with CD28 on T cells better than anti-CD28 antibodies, and that the B7:CD28 interaction leads to cytokine production and T cell proliferation, which in turn is involved in allograft rejection and graft versus host disease (see e.g., "USES" at columns 13-16). Linsley et al. teach that CTLA4Ig may be used alone or in combination with other immunosuppressants that block T cell proliferation in treating graft versus host disease (e.g., column 16, especially lines 18-21).

Thus Linsley et al. teach that reagents which inhibit T cell proliferation can be used in methods of treating both graft versus host disease and immune rejection of transplanted tissues or organs.

It would therefore have been obvious to the ordinary artisan at the time the invention was made that a method taught generically to inhibit activation of lymphocytes could be applied to the specific conditions of graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ. The ordinary artisan at the time the invention was made would have been motivated to apply the generic method recited in the claims USSN 09/383,551 to the specific conditions taught by Linsley et al. because Linsley et al. teach that T lymphocyte activation is a central feature of graft versus host disease and rejection of a transplanted organ or tissue.

Alternatively, the ordinary artisan at the time the invention was made would have been motivated to provide a method of treating the specific conditions of graft versus host disease and rejection of a transplanted organ or tissue wherein the method comprised both the claimed anti-AILIM antibody and the reagents taught by Linsley et al. because Linsley et al. teach that combination therapy with other reagents that inhibit T cell proliferation is routine practice in the art for providing new and improved methods of preventing or treating graft versus host disease and rejection of a transplanted organ or tissue.

The ordinary artisan at the time the invention was made would have had a reasonable expectation that the method claimed generically in the USSN 09/383,551 could also be used in a method of preventing or treating graft versus host reaction or immune rejection accompanying graft versus host reaction or transplantation of a tissue or organ because the activation of lymphocytes is a central feature of graft versus host disease and rejection of a transplanted tissue or organ, as taught by Linsley et al.

The individual cytokines interferon γ and interleukin 4 would necessarily be inhibited in any method comprising contacting the AILIM polypeptide of SEQ ID NO:2 in vivo with an antibody that inhibited activated T cells. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

*This is a provisional obviousness-type double patenting rejection.*

22. Claims 18-22 are directed to an invention not patentably distinct from claims 55-63 and 90-94 of commonly assigned USSN 09/383,551 for the reasons set forth supra.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned USSN 09/383,551, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

***Conclusion***

23. No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
June 11, 2003

PHILLIP GAMBEL
PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
6/11/03